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Vol. XL No. 10

ALBANY MEDICAL ANNALS

Journal of the Alumni Association of the
Albany Medical College

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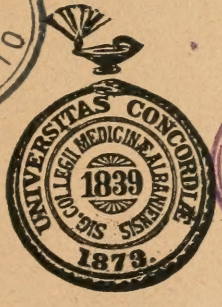

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ALBANY MEDICAL ANNALS

Journal of the Alumni Association of the Albany Medical College

EDITED BY
J. MONTGOMERY MOSHER, M. D.

Published on the First of every month
Subscription Price, Two dollars per annum in advance
Advertising Rates given on Application

Address all communications to ALBANY MEDICAL ANNALS,
Albany Medical College, Albany, N. Y.
Entered as Second Class matter at the Post Office, Albany, N. Y.

Acceptance for mailing at special rate of postage provided for in section 1103, act of October 3, 1917, authorized July 31, 1918

Vol. XL, No. 10 October, 1919

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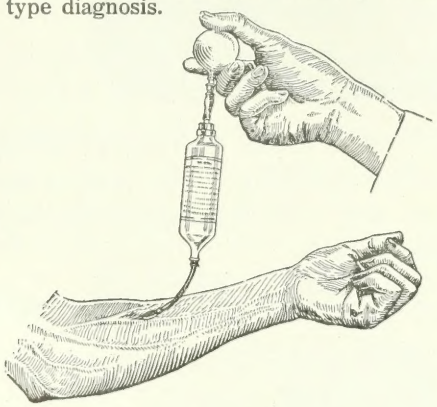

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Publisher's Department

PROPHYLAXIS OF INFLUENZA.—If we may judge the future by the past, there is likely to be a recurrence this fall and next winter of the influenza epidemic which resulted in the death of nearly half a million persons in this country a few months ago. In the event that this forecast proves true, what can physicians do to limit the spread of the disease and lessen its terrors?

Immunization with a reliable vaccine would seem to offer the best solution of the problem. Clinical reports on the use of preventive vaccine, as published in various medical journals in recent months, warrant this conclusion. Three instances are here cited:

In Cleveland, Ohio, last spring 3,427 prophylactic injections of influenza vaccine were given to the employees of a large manufacturing plant. Of those who received one injection, 378 developed the disease; of those who had two injections, but 37 were affected, while of those who received the full course of three injections, only three contracted influenza. Of the whole number attacked, seventeen died. Eleven of these had not been treated prophylactically, while the remaining six had had but one injection.

In the Kentucky *Medical Journal* for May, 1919 (page 199), the editor says: "The reports from some three hundred thousand cases indicate that the vaccine (Rosenow) decreases influenza, almost entirely prevents pneumonia, and in practically no case where it was used had death occurred."

In the *Canadian Medical Association Journal* for June, 1919, Major F. T. Cadham, C.A.M.C., reports his observations on the use of preventive vaccine in the influenza epidemic in Winnipeg. He says: "I believe the vaccine used as a prophylactic for the members of the Canadian Expeditionary Force of this district to have been of value. The incidence of pneumonia was less than one-half and the mortality rate less than one-fourth in the inoculated, as compared with the uninoculated, admitted to the special hospital under similar conditions."

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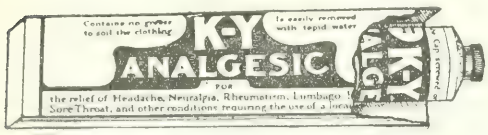
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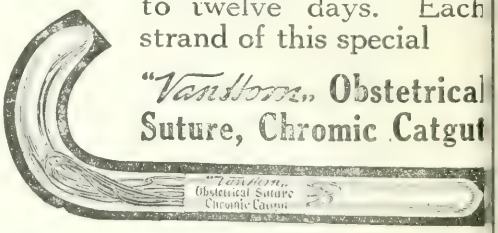

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VOL. XL OCTOBER, 1919 No. 10

ALBANY MEDICAL ANNALS

Original Communications

THE NEUTROPHILIC GRANULES OF THE CIRCULATING BLOOD IN HEALTH AND IN DISEASE. A PRELIMINARY REPORT.

Read at the Annual Meeting of the Medical Society of the State of New York, at Syracuse, May, 1919.

BY G. S. GRAHAM, M. D.

(From the Pathological Laboratories of the Albany Hospital and the Albany Medical College)

The cytoplasmic granules characteristic of the myeloid cell series occur in the circulating blood of man as three types, neutrophilic, eosinophilic, and basophilic. It is probable, however, that only the first two of these types should be considered as true granules in the strict sense of the term. In a paper to appear elsewhere evidence is brought forward that is believed to indicate strongly that the gamma granule is derived from the eosinophilic and rarely perhaps from the neutrophilic type through some obscure change in the granular substance presumably of a degenerative nature. Under this conception the type represents only a physiologically inactive pseudo-granule and its containing cell, the basophile, is not a functionating leucocyte but a degenerating cell probably having no part to play in the general scheme of normal leucocytic activity. The eosinophilic leucocyte participates only to a minor degree in the disturbances of leucocytic equilibrium excepting in a few well recognized conditions of somewhat special type and it is evident that the irritants capable of mobilizing it form a restricted group of noxious substances. The neutrophile remains then not only

as the form numerically predominant in normal blood but also as the most active of the granulocytes in a physiological sense. Upon it falls the main burden of the protective response to toxic conditions affecting the local or general bodily metabolism and the study of the leucocyptic reaction to various acute inflammatory conditions is largely a study of the neutrophilic variation.

During the past twenty years much attention has been devoted to the study of the blood changes consequent upon infection. On the cytologic side such study has concerned itself very largely with the numerical fluctuations in the leucocytes. At first only the "total" leucocyte count was used but this was soon supplemented by the more informing "differential" count and then the correlated study of both these factors appeared as an attempt at the more exact definition of the principles underlying the phenomena of leucocytosis. Despite the great value of these studies both in the general information derived from them and in the more immediate value of their results as practical and valuable aids in determining questions of diagnosis and prognosis there still appear many unexplainable discrepancies between the conclusions drawn from the blood count and the clinical course of infectious conditions. And it is not to be wondered at that such discrepancies should occur. So far as analogy is concerned, it is after all somewhat surprising that we should expect so much from the mere enumeration of the cells in the circulatinig blood, for such observations leave out of account almost entirely any consideration of the finer morphologic changes that may take place in the cells of the type most concerned in the cellular reaction that is taking place. The blood is a tissue and the tissue microscopist would scarcely draw any conclusions from an examination of a section in which he had merely counted the number of cells without at the same time noting any changes discoverable in their morphologic appearance. The body tissues in general exhibit characteristic reactions to stimuli that are entirely comparable with those that may be observed in the blood but the character of the reaction, the intensity of the stimulus provoking it, and the probable end result of the phenomena set in motion are indicated not by the number nor by the relative percentage of the various cells present so

much as by the morphologic changes evident in the individual cells of the type most concerned. While the analogy cannot be carried over intact into hematology it may still serve to illustrate the point that we should search for some factors of leucocytic variation other than the merely numerical ones to serve us as guides in the interpretation of the varying blood picture found in disease conditions.

Arneth suggested a morphologic factor when he proposed his "nuclear index" as a basis for the interpretation of the leucocytic response to infection. He postulated that the relative age of a given neutrophile may be judged according to the number of segments exhibited by its nucleus. The nucleus of the earliest or youngest leucocytic form as it enters the blood from the bone marrow is a single mass. This mass subdivides into two, three, four and finally five or more lobes as the cell grows older. Starting from this point he determined what he believed to be the "nuclear index" of the normal blood, pointed out what he believed to be the effect of toxic conditions in causing a relative increase in the younger cell forms and maintained that in a given case of infectious disease, and particularly in tuberculosis, the degree of toxemia present may be judged according to the extent of the relative increase in the cells of the single or bi-lobed nuclear types. The validity of Arneth's fundamental conception has not been seriously questioned and the conclusions based upon it appear to be essentially sound but the nuclear index has not received any general acceptance as a practical aid in clinical work despite the fact that it is usually admitted, even by those reporting doubtfully or unfavorably upon its use, that the indications derived from it may occasionally be of distinct value both in diagnosis and in prognosis.[2] Here again it is not surprising that the unsupported figures of the Arneth index should prove misleading in some cases for we can hardly doubt that there is much more to the mechanism of leucocytosis than the mere question of the age of the individual cells.

Continuing the classical analogy a moment longer, may it not be that we should investigate not only the number of our troops, not only their average age but also their physical condition or fitness? Should we not, in other words, attempt a study of the finer

morphologic changes that may occur under conditions of disease not so much in the nucleus as in the cytoplasmic structure? From analogy with the general facts of cellular changes everywhere observed as the result of the action of stimulative or destructive agents upon the body cells it would be logical to expect that the active and highly sensitive neutrophile should show degenerative cytoplasmic changes as the result of the action upon it of stimuli capable of exciting it to the degree evident in well developed cases of hyperleucocytosis. However active may be the withdrawal of damaged cells from the circulation it would seem unlikely that the laboring organism of severe infectious toxemia can maintain its circulating leucocytes intact. Reports of observations bearing upon this point are not lacking in the early literature. Cytoplasmic as well as nuclear degenerative changes were reported by the pioneer workers in hematology. In general these were interpreted as evidences of peptization, coagulation or disintegration of reticulum or hyaloplasm. Added to them were changes affecting the characteristic granules of the marrow cell series. These might consist merely of changes in the staining reaction toward aniline dyes or the granules might disappear in whole or in part. It is still accepted that degenerative changes of these general types may occur in the cells of the circulating blood in myelogenous leukemia but for the most part hematologists have ceased to give them more than passing attention in the case of the leucocytoses proper. Occasional references to certain of these changes do continue to appear but for the most part there is an attitude of scepticism toward their recognition. This is due no doubt to the realization that such conclusions must be drawn cautiously when they are based merely upon the study of the cells in blood smears. No matter how careful the technic employed in its preparation it is practically impossible to avoid artefact production in the blood film and added to this difficulty there is the further handicap that the stains in common use are notoriously capricious in their action. This variability in the stain works particularly against the satisfactory study of the granules.

But it is exactly in this particular of a successful granule staining that the so-called oxidase or peroxidase methods promise

to prove of value and the striking emphasis laid by them upon the granular content of the neutrophilic cytoplasm inevitably suggests the desirability of reopening the old question as to whether or not changes may be demonstrable in these granules under various conditions of infectious or non-infectious toxemia.

Little is known as to the nature or purposes of the leucocytic granules. They were regarded by Ehrlich as reserve material stored in the cell for eventual use in the processes of cellular metabolism and on the other hand they have been regarded by others as some extraneous material having no vital connection with the cell life or as excretory substances the product of katabolism. Again they have been considered as of secretory nature, representing a substance specifically elaborated by the cell and having some definite part to play in its general or special physiological activities. Hankin saw in them the source of the alexins and this idea has been favorably received by other workers. While there is nothing beyond inference and analogy to support one or another opinion as to just what rôle is actually played by the granular substance, the idea that it is concerned in some more or less direct way with the antibacterial or antitoxic defense is at least most attractive. Very marked changes in the granules may readily be determined by the study of leucocytes engaged in phagocytosis, as for example in opsonic preparations or in smears of pus. Smears from an active case of gonorrhea are very satisfactory. When such preparations are stained with a "peroxidase" reagent interesting examples of the more or less complete disappearance of the granules from individual cells may be obtained. While exceptions may occur, it may be stated in general that the granules disappear from the leucocytes progressively as the number of bacterial inclusions in the cell increases. The significance of this granular failure is not clear. It might be explained, perhaps, on the basis of any of the above theories of granular significance and it may merely indicate a change in the hydrogen ion concentration of the cytoplasm consequent upon phagocytic activity but it seems not impossible that a careful study of the phenomenon might provide a possible starting point for a morphological study of the mechanism involved in phagocytosis that might approach the question

from a direction somewhat different from those previously followed.

In the benzidine method of granule staining the benzidine may be said to act toward the granular substance as a color indicator. When it is applied to the leucocytes in the presence of traces of hydrogen peroxide a reaction takes place as a result of which a permanent brown dye is set up and this becomes fixed in or upon the granule mass. Simple counterstaining completes the procedure necessary for a satisfactory cytological preparation. The method has been described elsewhere[6] but may be summarized briefly as follows: the perfectly fresh smear is fixed for a few seconds in a fresh mixture of one part of forty per cent formaldehyde in nine parts of ninety-five per cent alcohol; washed in water; and stained for five minutes in the benzidine solution. This is made up freshly as used by adding a few crystals of chemically pure benzidine (the Merck preparation has been used) and 0.02 cubic centimeter of an active hydrogen peroxide (U. S. P.) to 10 cubic centimeters of forty per cent alcohol. Or, although this is somewhat less desirable, a two-tenths of one per cent solution of benzidine in forty per cent alcohol can be made up in sufficient quantity for one or two weeks' supply and the peroxide can be added to small portions of this stock solution as they are withdrawn for use. Five minutes has been adopted as the standard staining time. The preparation is now washed thoroughly under the tap, counterstained, washed in water and dried. Methylene blue was originally recommended as the counterstain but this has been replaced in recent work by the Futcher-Lazear carbol-thionin, which gives a sharper nuclear stain and a more pleasing color tone to the slide in general. It is made up by adding 20 cubic centimeters of a saturated solution of thionin in fifty per cent alcohol to 100 cubic centimeters of a two per cent aqueous solution of phenol. The mixture should be allowed to stand for a day or two before being used. A sharp stain may be obtained in one to two minutes.

Long exposure to the benzidine solution will result in a slight diffuse brownish coloration of the erythrocytes and possibly of the megakaryocytes of the bone marrow but no other evidence

of a non-specific staining of any of the body cells has been observed under the technic employed for blood smears or tissues. On the other hand, great emphasis is laid upon the cells of the marrow series. These stand out in bold relief so that they lend themselves well to morphologic study. Since also the granular staining appears to involve a distinct chemical reaction between some granular or cytoplasmic constituent and the indicator or staining agent and is not merely the less specific combination between a dye and some coagulated cellular material such as is made use of in the usual histological methods, the present procedure would seem to offer a certain amount of evidence as to the vital condition of the granule or its containing cell.

The position here taken, it may be pointed out, does not commit us to any dogma as to the nature of the granular substance nor as to the ultimate explanation for the reaction in question. The leucocytes are credited with harboring a rather formidable array of enzymes. Whether the observed reactions on which these claims are based are due in every case to enzymatic activity or merely to the influence of "unorganized" catalysts of organic or even in some cases of inorganic nature is not certain. So far as concerns the substance responsible for the color reaction that we are considering, the general characteristics exhibited by it, including its susceptibility to the action of certain physical and chemical agents such as dry heat, sunlight, acids and alkalies, concentrated alcohol, mineral salts, etc., are much like those of the true enzymes, but there are still weighty considerations against its unqualified acceptance as such a body. It is uncertain whether this substance does or does not form a part of the granule mass proper. Presumably it does, but nothing is known certainly as to the facts of the case. Finally, it has been questioned whether we are justified in holding to the older assumption that the reaction involved is one of direct oxidation of the indicator by the granular substance. All these questions are of interest and their solution may go far toward clearing up many questions relating to the leucocytes and their activities, but for our present purposes we may disregard them while holding merely to the empiric observation that under the conditions

named above it is possible to stain the leucocytes in such a manner that their granules are prominently displayed.

An examination of the leucocytes in normal blood as stained by the benzidine method will show that not all the neutrophiles appear equally supplied with granules. The cytoplasm of the individual cell may be densely crowded with them; again they may appear in a more open pattern; while in other cases more or less well defined columns or fields of empty cytoplasm may shine through between the opaque clumps or chains of stained particles. In disease some of the cells may show very few granules or may even be entirely devoid of anything but shadowy remnants of them. Comparable changes occur within the tissues in acute inflammatory exudations.

The questions suggested by this variation in the granular quota of the individual leucocytes and particularly the marked changes occasionally seen in severe infectious toxemia led some time ago to an attempt at the experimental production of granular changes in the blood of animals. The animal chosen for the work was usually the white rat since his leucocytes approach those of man in their granule characteristics more closely than do those of the other small laboratory animals. In the guinea pig and rabbit the "special" granules are few and scattered even in the normal polymorphonuclear cell and it is difficult to determine changes in them. Benzol was first chosen as a toxic agent that might be expected to have some direct action upon the leucocytes. It was given by subcutaneous injection to seven rats and by inhalation to three. In spite of heavy dosage and continued treatment no leukopenia such as is characteristic of the benzolized rabbit was obtained in the injected animals excepting to a minor degree in one case, nor were any undoubted granule changes determined. There was possible granule failure in the inhalation-treated animals and in one of these that succumbed after daily exposure for twenty-five days there was a terminal white count of 3,300 and an apparent deficiency of reacting granules in the cells of the bone marrow. A benzol leukopenia was obtained in two rabbits but no decided granule changes could be made out in the leucocytes of the circulating blood. Similar failure attended the exposure of rabbits and

guinea pigs to chloroform narcosis as well as the treatment of white rats with heavy doses of the X-ray. Somewhat more encouraging results followed the subcutaneous injection of a hemolytic streptococcus and of a freshly isolated staphylococcus into a small series of white rats. The subcutaneous injection of a non-fatal dose of streptococcus was sometimes followed in one or two hours by a definite failure of the granules in the circulating leucocytes while with recovery from the toxemia the granules reappeared in unusual numbers. On the whole, however, the technical difficulties encountered were found to interfere with any satisfactory study of the blood picture, particularly in regard to the relation of the suggested granule changes to the numerical fluctuations in the white count and the polymorphonuclear percentage, and the study was abandoned. The experimental work thus briefly summarized was carried on two and three years ago. The staining method then employed was probably not so well adapted to its purpose as the one now used and the extent of the granule change that may be expected to occur was perhaps conceived of as greater than would now be demanded. It is possible that a repetition of the experiments might now yield more illuminating results, but at the time these were judged to be too inconclusive to warrant further trial and the added technical difficulties referred to were sufficient to discourage continued work along the experimental line. Instead, such time as could be found has been devoted to a study of human blood in various disease conditions and, with this more favorable material, an attempt has been made to formulate some basis of judgment as to whether any definite changes can be detected.

The difficulty that at once arises in any such attempt lies in the discovery of an adequate standard of measurement. The ideal method would of course be that of an extraction of the reacting substance from the leucocytes in a known volume of blood and the exact determination of its value by a suitable reagent. Some attempts were made to approach the problem from this side, but these were entirely unsuccessful. Kastle and Amoss[8] made a somewhat similar attempt some years ago but concluded that the variable peroxidase values shown by the

blood in different diseases were due merely to the variable hemoglobin content present. Since also, as stated above, the exact nature of the color reaction involved is entirely unknown, it seemed for the present more logical to treat the problem purely as one of morphological histology and to attempt a numerical estimation of the extent to which the leucocytes in a given case may have suffered changes in their morphological appearance. Occasional record of previous studies along this line has been encountered in the literature. Klopfer,[9] using the original Winkler-Schultze oxidase method, studied the tissues from cases of poisoning with gas, hydrocyanic acid, phosphorus, etc., without finding evidence of any change from the normal cellular reactions in the parenchymal cells of fresh unfixed organs. Hatiegan[7] also used the Winkler-Schultze method in studying the blood in various infectious conditions and concluded that no changes in the leucocytes could be made out. Fiessinger and Rudowska[5] noted the variable granule content in the individual neutrophiles of blood smears stained by their benzidine method and divided these cells into two groups according to the relative abundance of their granules. They state the normal ratio of these groups as 6% of the + or deficient cells and 94% of the ++ or fully granulated forms. The latter vary from 84% to 94% in a series of nine diseases listed, these including pneumonia (94%); acute articular rheumatism (86%); rabies (85%); mitral regurgitation (84%); chronic nephritis (94%); acute meningitis (86%). A group of diseases with "diminished reactions" consists of typhoid fever (+26%, ++74%); pulmonary tuberculosis (+55%, ++45%); and purpura (+36%, ++64%). They believed that the granule constitutes a "pivot of reaction about which is concentrated a large part of the leucocytic metabolism" and concluded that the observed loss of granules in varying percentages of the neutrophiles in some of the diseases studied indicated a diminished oxidizing capacity on the part of the cells affected and therefore a valuable index of the general bodily condition.

For the present study the neutrophiles were arbitrarily divided into four types according to the abundance of their reacting granules. Type IV was taken as the normal. Here the granules

are abundant and heavily stained. They may be so closely crowded within the cell body as to mask the enclosing cytoplasm almost completely. More often, however, particularly in thin smears such as must be used for satisfactory study, the individual granules may be distinguished. They may be scattered uniformly through the cell or may show a beaded arrangement as short chains sometimes disposed radially in certain sectors of the cytoplasmic body. In the lower members of the group traces of clear cytoplasm may be seen about the nuclear membrane and between the rows or clumps of granules or even about the individual granules, but on the whole the granules impress one as being compact in their arrangement, rather uniform in size and appearance and arranged in a regular pattern that fills the cell body. Type III shows slight deficiency of the granules. The separation of the stained particles into five or six distinct groups or fields suggested in some of the lower Type IV cells has now become prominent so that the cell body presents distinct granule-filled sectors outlined by lanes of relatively clear cytoplasm. In the wider portions of the cytoplasmic body the fields may be clearly wedge shaped with centrally disposed apices but in the narrower portions of the cell along the convex surfaces of the nucleus they become flattened peripherally and lose the wedge shape. There is a distinct perinuclear halo and small irregular "bald" areas make their appearance particularly in the marginal cytoplasm normally occupied by one of the smaller granule fields. The granules may appear scattered and somewhat understained or may show a patchy variation in size and depth of color. Scattered heavily stained masses may appear that are noticeably larger than the usual forms and have a hazy outline. These hazy or smudgy bodies are perhaps the result of degenerative changes in the granular substance, their characteristic appearance being shared by an increasing percentage of the granules in the cells of the lower types to be described. In Type II there is undoubted loss of reacting granular material. The class has been considered as including cells varying at the top from those showing well marked axial core remnants of the fields typical of Type III down to forms in which only a few of the more central granules of these axes remain in place, the remnant

granules occurring as isolated groups whose location suggests the original field pattern. Again, all but one or at most two of the fields may have become unrecognizable or may be represented only by a vague, diffusely stained, apparently non-granular material. The one or two remaining fields may have a fairly abundant residue of the original granule quota. Type I shows only a few vaguely reacting granule shadows without any suggestion of definite pattern arrangement or the reacting substance may be represented only by a diffuse brownish haze in portions of the cytoplasm. The nuclei in the latter two types often stain faintly.

To summarize:

Type IV is a cell with a maximum granule quota. The pattern is regular and uniform.

Type III is a cell with such slight granule deficiency as may be found in fair percentage in the cells of normal blood. The granules may appear scattered and rather understained but usually show a well-marked field arrangement and sometimes irregularities in the size and staining of the individual particles. Small areas of cytoplasm may be distinctly bare of granules particularly in the marginal portion of the cell.

Type II shows undoubted granule loss. This may be general so that only a skeleton of the field pattern persists or it may affect individual fields unequally and one, or at most two, of the groups may be fairly well preserved while the remainder of the cell body is practically bare of reacting substance.

Type I shows complete or almost complete loss of granules.

Working on the basis of this tentative and very arbitrary grouping of neutrophilic types, a preliminary survey was made of the blood from a number of apparently healthy young adults, for the most part students. The cells were classified not only according to their granule content but also with respect to their nuclear configuration or "Arneth index" values. The latter grouping was included in this survey and also in some of the counts made later on pathological blood because it was thought that it might offer some check on the granule findings, at least until such time as it might be determined with some reasonableness whether, in the first place, any granule changes are to be

expected in mild or severe cases of toxemia, and, secondly, if such changes did appear, what their possible relation might be to another suggested factor of leucocytic variation.

TABLE 1. GRANULE AND ARNETH INDICES IN APPARENTLY HEALTHY YOUNG ADULTS

	GRANULE TYPES				ARNETH TYPES				
	IV	III	II	I	1	2	3	4	5
1	96	4	0.6	0	16	29	44	9	2
2	94	6	0	0	12	28	44	13	3
3	90	10	0	0	8	27	45	18	2
4	89	11	0	0	7	30	46	16	1
5	88	12	0.3	0	9	22	50	17	2
6	88	12	0	0	5	26	53	15	1
7	87	13	0	0	9	29	48	12	2
8	80	18	2	0	15	28	45	11	1
9	77	23	0	0	11	38	41	10	0
10	77	21	2	0	16	25	39	18	2
11	75	23	2	0	8	33	47	11	1

Table 1 presents the preliminary series of counts that were made on healthy individuals. The series is of course too small at present to allow any final conclusion to be drawn from the results obtained and it is, in any case, difficult to appraise the value of figures arrived at as these must be. They can be regarded at the best only as approximations and further experience may modify the impression gained from them. But in general it would appear that cells of Type I are not to be expected in normal blood and that those of Type II occur but rarely. There is rather wide variation in the proportionate numbers of Type IV and Type III cells. The significance of this is not clear. The impression has been gained that there may be some correspondence between the Type IV percentage and the robustness of the individual from whom the blood was obtained, the more vigorous and possibly more resistant subjects being most apt to show the higher Type IV averages. This, however, needs verification. There is some question whether the last three counts given in the table should be regarded as normal although the subjects from whom they were obtained complained of no illness.

Two other controls originally accepted as "healthy" showed counts of a parallel order. One of these, a vigorous young man with a granule count of 79-21-0-0, was found to be suffering an intestinal disturbance accompanied by slight malaise. The other, presenting a count of 73-25-2-0, was undergoing an exacerbation of a chronic sinusitis. It does not necessarily follow, of course, that moderately low counts are to be explained definitely as the result of slight infection for there may be other factors entering into the regulation of the individual granule count. Cooke[3] thought it probable that the Arneth index may vary in different healthy subjects although maintaining a constant level for any given individual and the same may be true of the granule index. On the whole, it seems probable that a Type IV percentage of 80 or over with practical absence of Type I and Type II varieties may be taken as most likely to outline the range that is to be expected in normal blood. If we accept the first eight counts of Table 1 as meeting this tentative standard, the averages obtained are, for Type IV, 89%; for Type III, 11%. For the same specimens the averages for the Arneth types are, in order, 10.1-27.3-46.8-14-1.75. In counting the nuclear segments the attempt was made to follow the simple standard of judgment stated by Cooke and despite the very considerable differences in the individual counts of the present table the averages obtained are curiously like those obtained by him in the blood of eighty normal adults, viz., 10.9-25-46.7-15.3-2.1. Arneth's original figures were 5-35-41-17-2. The sum of the nuclear groups 1 and 2, which is the indicator value actually used in drawing conclusions from the count, becomes in the three results, respectively 37.4; 35.9; and 40.

Thin smears must be used in making the counts. This precaution is important for obvious reasons. In making the granule grouping only intact cells have been counted. A varying number of cells always found in the blood film show, under the usual stains, a more or less faintly outlined atypical nucleus and a shadowy cytoplasm. They have been considered by some writers as degenerated cells and by others as pure artefacts. With the benzidine method the granules of such cells are irregularly stained and more or less deficient and the whole appearance is distinctly that of degeneration. In view of the doubt as to their signifi-

cance, however, it was not deemed best in this preliminary work to include such forms definitely as neutrophiles of one or another type. Only those cells showing compact body and definite outline have been recorded in the counts. The so-called "large mononuclear" leucocyte appears to contain a few weakly reacting granules or a considerable number of them. It must not be confused with a neutrophile bearing a single nucleus. The differentiation is sometimes difficult and the cell becomes a stumbling block here as in other methods. The eosinophile is readily recognized from the large size, sharply globular outline and obvious refractivity of its granule. Owing to the water solubility of the gamma granule, the basophile or mast cell appears as an atypical polymorphonuclear cell with faintly stained cytoplasm showing no structural detail or only a vaguely suggested vacuolation.

TABLE 2. GRANULE AND ARNETH INDICES IN INFECTIOUS AND NON-INFECTIOUS TOXIC CONDITIONS.

	GRANULE TYPES				ARNETH TYPES					
	IV	III	II	I	1	2	3	4	5	Remarks
1. Tubercular peritonitis	30	60	10	0	18	43	31	7	1	
2. Tubercular osteomyelitis	34	55	11	0	25	46	20	9	0	
3. Typhoid fever	4	14	57	25	47	37	14	2	0	Fourth week. Recovered.
4. Diphtheria	76	24	0	0	13	42	31	11	3	2nd day. W. B. C. 17,000. 12,000 units antitoxin given during previous 18 hours.
5. Acute alcoholism	35	54	11	0	17	42	40	1	0	
6. Uncinariasis	44	48	8	0	2	17	38	39	4	
7. Trichinosis	2	24	56	18	32	47	14	7	0	Moribund. W.B.C. 5,000. Eosinophiles, 1%.
8. Trichinosis	20	56	24	0	22	45	29	4	0	Third week. Recovered. W.B.C. 12,000. Eosinophiles, 26%.
9. Trichinosis	19	42	37	2	53	33	13	1	0	Third week. Recovered. W.B.C. 20,000. Eosinophiles, 23%.

The counts given in Table 2 are in part from selected cases. That is, the primary question has been that of whether any granule changes can be made out in toxic conditions and, if made out, whether they can be recorded in such a way as to offer a standard of comparison for a particular case or a particular disease. While smears from all available toxic and many non-toxic cases have been examined, therefore, and rough judgment made as to whether or not any granule change could be made out, only those cases were selected for actual count which were most clear cut on the clinical side and which showed a neutrophilic change considered as of particular interest. Thus, the two cases of tubercular infection tabulated should naturally be accompanied by counts upon cases of pulmonary disease. As a matter of fact a small series of smears from cases under sanatorium treatment have very recently been obtained. No obvious changes were apparent in them on mere inspection excepting in two advanced cases with active lesions. None of these cases has been charted, the more careful study of these as well as other conditions being reserved for a later time when it is hoped that a more detailed report may be made. The single count recorded for typhoid fever shows a granule deficiency more marked than had been expected. The extreme degree of the calculated change is of interest in the light of the subsequent history of the case, which appears to have been that of an uneventful recovery. But one case of diphtheria has been encountered since the method of granule charting was adopted. The patient showed no evidences of toxemia when the blood was examined shortly after entrance into the hospital. It would be highly desirable to secure further counts on toxic cases in view of the granule changes described in this disease many years ago by Ewing[4] and considered by him at that time as a valuable clinical sign of the patient's condition. The three cases of Trichinosis charted were seen in a hospital during a small epidemic of the disease. Cases 9 and 10 of the table were severely ill but eventually recovered. Case 8 died about twenty-four hours after the blood examination was made. Case 7 is introduced as an example of another parasitic disease. The patient was a young West Indian negro presenting

no clinical symptoms beyond the characteristic anemia and listlessness.

Acute lobar pneumonia has shown the most striking neutrophilic changes of any of the diseases studied. Here the variation in the morphology and staining reaction of nucleus and cytoplasm is apparent in the neutrophiles of preparations stained by the usual eosinate of methylene blue mixtures and even the granule changes may be appreciated. Thus on the basis of an exhaustive study of the disease conducted at the Rockefeller Institute, the statement is made[1] that "the appearance and staining qualities of the white blood cells often reflect the condition of the patient. . . . The nuclei of the (degenerated polymorphonuclear) cells appear fragmented, stain poorly, and the cytoplasm presents an appearance suggesting cloudy swelling. On the other hand, a day or two before crisis, . . . there may appear many polymorphonuclear cells . . . (whose) cytoplasm is packed with well staining coarse granules." The present series of cases is too limited to allow of anything more than tentative conclusions but in general the evidences of leucocytic disintegration reported are fully supported by the findings in benzidine-stained preparations. In cases doing badly there is a marked failure in the number of reacting granules and in the intensity of the color reaction in the surviving ones. This is probably the benzidine picture of the change suggesting "cloudy swelling" in the report quoted. The nuclei stain poorly and there is a decided "shift to the left" in the Arneth index.

Case 1 of Table 3 was one of the first in which the indices were calculated. The patient, an Italian laborer, was admitted to the hospital toward the end of the epidemic of last fall. He was suffering an acute attack of perfectly typical post-influenzal pneumonia. The blood smears, taken about twelve hours before death, show complete absence of Granule Type IV cells while 22 per cent were reckoned as of Type I. In the fatal Case 2, there is a decided drop in the granule values during the final forty-eight hours of an acute lobar pneumonia, the total leuco-

TABLE 3. GRANULE AND ARNETH INDICES IN PNEUMONIA AND ITS SEQUELAE

	GRANULE TYPES				ARNETH TYPES					
	IV	III	II	I	1	2	3	4	5	Remarks
1. Pneumonia, post-influenzal	0	27	51	22	36	40	16	8	0	Died same night.
2. Pneumonia, acute lobar	57	42	1	0	15	38	29	12	6	W. B. C. 24,800.
	17	47	32	4	30	28	32	9	1	Same case, two days later. W. B. C. 25,900. Died same night.
3. Pneumonia, double acute lobar. Protracted course	15	53	31	1	20	45	28	7	0	Type IV and streptococcus.
	11	41	34	14	29	38	26	6	1	Same case. Four days later. W.B.C. 5,260.
	11	51	29	9	34	40	20	6	0	Eleventh day Temp. normal. Liquid diet, W. B. C. 5,600.
	51	46	3	0	29	33	28	10	0	Eighteenth day. W. B. C. 8,420.
4. Pneumonia, delayed resolution. Empyema	16	48	34	2	22	31	35	11	1	Boy, 14 years of age. W. B. C. 23,000.
5. Empyema, following post-influenzal pneumonia	13	57	29	1	20	38	33	9	0	Slowly convalescent.
6. Pneumonia, acute lobar	78	22	0	0	32	40	24	4	0	Moribund.
7. Pneumonia, acute lobar	90	10	0	0	19	40	25	15	1	Moribund.

cytes meanwhile holding a constant level. Case 3 was that of a farmer, 35 years of age, who had been seriously ill for two weeks previous to his entrance into the hospital. He presented a double acute lobar pneumonia with marked prostration. The white count was persistently low. He was dangerously ill for about a week, after which the temperature fell by lysis, reaching normal at the time of the third count recorded in the table. Despite the marked clinical improvement evident at this time, the granule count seems not to have undergone any material alteration. Distinct return toward the normal is shown, however, in the

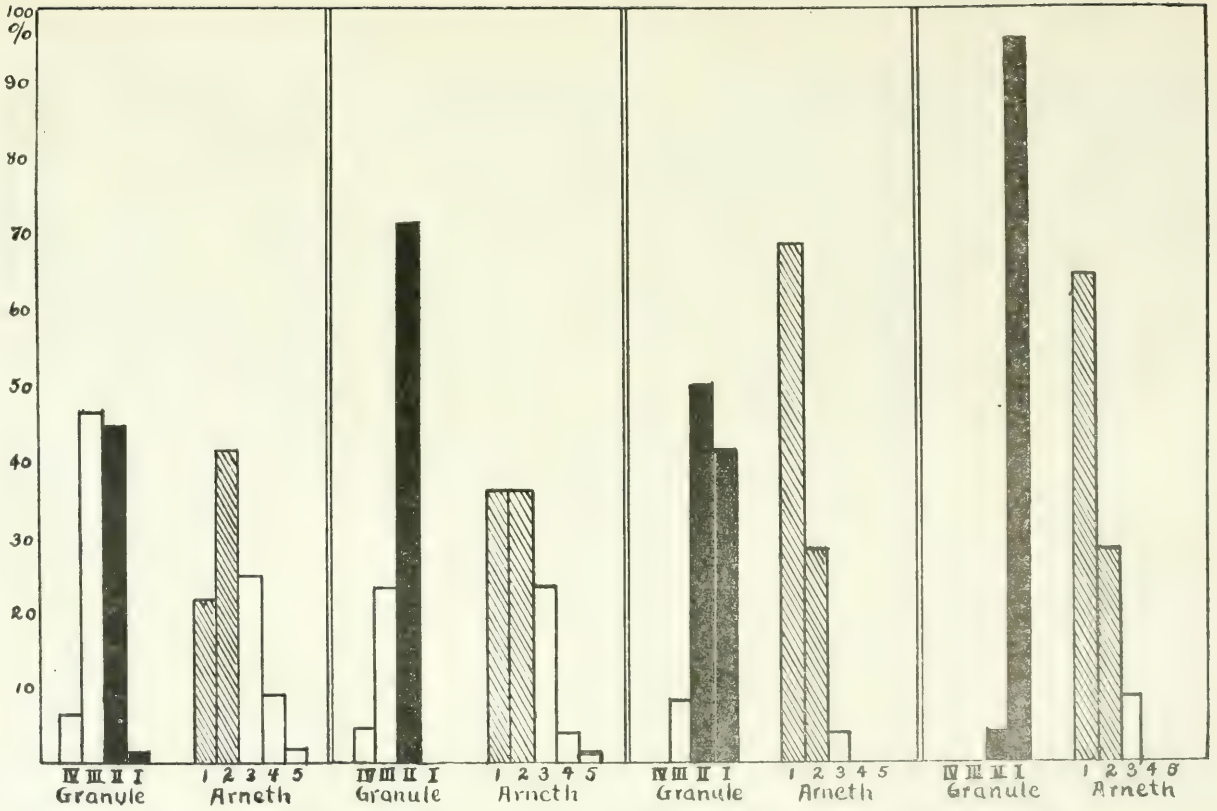

CHART — Granule and Arneth indices on successive days in a fatal case of acute lobar pneumonia (Type I). No response to treatment with homologous serum.

count taken one week later. The findings indicate the great desirability of a close study of a series of cases with the object of determining whether the curve of variation in the granule index may be found to present any recognizable changes preceding those in the clinical symptoms or whether they merely accompany or follow the latter. In other words, the question arises whether the index may constitute a symptom having prognostic value. Cases 6 and 7 indicate that, for the present, conclusions may be drawn from the granule picture only with the greatest caution. Both patients were brought into the hospital moribund. The blood smears, obtained within one and two hours before death, show in both a surprisingly high granule count. It might be argued that these are to be considered as cardiac deaths occurring, in a sense, as accidents, in patients showing extremely active leucocytic response to the infection, but such an hypothesis could be supported only by extended observation.

The most remarkable case encountered in the present series showed neutrophilic changes represented graphically in Chart. The patient was a well developed man of 31 years of age. He was markedly toxic from the time of his entrance into the hospital on the first day of the disease. The white count on entrance was 14,400. On the succeeding days it fell to 8,000 and finally to 6,000. Pneumococcus, Type I, was recovered from the sputum. One hundred cubic centimeters of antipneumococcus serum was administered on the second day, and the same amount was administered once on the third day and twice on the fourth day, so that the patient received, in all, 400 cubic centimeters of the homologous serum. So far as could be determined clinically the treatment had not the slightest influence in combating the overwhelming toxemia and the patient died late on the fourth day. The granule failure in this case is extreme. The Type IV cells fell from the original count of 7 per cent on the first day to 5 per cent on the second and completely disappeared on the third day. The Type III cells showed an initial percentage of 47 that fell to 23 on the second day, 8 on the third day, and 0 on the fourth or final day. On the day of death there were 96 per cent of Type I cells and 4 per cent of Type II.

Discussion.

Certain precautions are necessary in applying the benzidine method to the study of the neutrophilic granules. The blood smears used must be as fresh as possible, particularly when there is question of granule failure, since even the cells of normal blood may show perceptible decrease in the granular reaction within twenty-four hours after the films are made. This is particularly true if they have been exposed for any length of time to direct sunlight. It is possible that the blood of some individuals may show this change more quickly than that of others, and smears from cases of myelogenous leukemia several weeks old have been observed in which there was little if any decrease in the intensity of the reaction, but no conclusions can safely be drawn as to the granule reaction unless the smears are stained within a few hours at most after they have been made. For the satisfactory calculation of granule groups it is essential that thin smears be used. The compressed cells of a thickly crowded field show only a confused granule mass in which no details can be made out. Finally, the cells in the marginal areas of the smear must be disregarded. The loss of granular reaction is most rapid here and smears more than one or two hours old may show a normal staining of the cells in the main body of the surface while the neutrophiles in a peripheral zone one or two immersion fields in width may appear to be few or entirely absent. Particular care must be exercised also in the staining, first, as concerns the solutions employed and, secondly, in the time of exposure to them. When the benzidine method was first used occasional difficulty was encountered that appeared to depend upon some variation in the fixing solution, but this has been absent since neutralized formalin has been used in preparing it. A potent source of trouble lies in the use of an inactive hydrogen peroxide. This may be avoided by occasional titration of the reagent to assure its content of available oxygen. Old benzidine-peroxide solutions give a quicker and deeper color reaction than fresh ones so that fresh mixtures must be used as the basis for any comparative study of the granular reactivity. An alcoholic solution of benzidine containing no hydrogen peroxide remains constant for several weeks and it is possible to

utilize this fact by making up solution sufficient for one or two weeks' supply, simply adding the appropriate amount of peroxide to small portions as they are removed for use, but for the most part the preparations serving as a basis for the counts recorded above have been stained with a solution not over six to eight hours old. An equivalent precaution that is highly important lies in the adherence to a standard benzidine staining time of five minutes. This is sufficient to demonstrate all granules that may reasonably be considered as normal. It fails to show any but a vague reaction or presents none at all in the case of certain granules such as may be found in the cells of pathological blood and which have been considered as abnormal. But prolongation of the staining time to ten or fifteen minutes may apparently result in a positive reaction on the part of some, at least, of these forms and it results also in a loss of detail in the granule picture, as though there were some diffusion of the stain through the enveloping cytoplasm. The first change that takes place in the progress of what has been considered as granule failure appears, therefore, to result merely in a lessened activity on the part of the property responsible for the benzidine reaction, although there may finally be complete absence of any demonstrable reaction. In view of the several possibilities of error pointed out, constant control should be exercised through the simultaneous staining of smears of known normal blood along with those whose granule content is to be determined.

The possible relationship of granule changes to variations in the total white count and the polymorphonuclear percentage has been touched upon only incidentally in the cases thus far studied but it is planned to take up this question in the work now being continued. There has seemed to be a general correspondence in the figures obtained for the granule and for the Arneth indices, this consisting in an increase of the cells of the lower granule types coincidentally with increase in the younger Arneth forms. But while this correlation has provided a certain amount of confidence in the validity of the present hypothesis that granular failure may take place in toxic conditions, it is doubtful whether continued Arneth counting will justify the time that must be spent upon it. This is particularly true in view of the fact that the thionin-stained nuclei are not as satisfactory for the work

as those provided by the usual blood stains and considerable time and effort must be expended in determining the nuclear type of many of the cells encountered, especially in pathological blood. It is probable that the correlation of granule changes, total white count and polymorphonuclear percentage offers a more practical line of study.

In cases of extreme granular failure such as have been encountered in pneumonia it appears probable that the granular deficiency evident in the leucocytes of the circulating blood may extend back into the bone marrow, since in some cases smears of this tissue appear to react less vigorously than the normal. The myelocytes as well as such leucocytes as may be present share in the granule loss. The phenomena involved here may be concerned in the problem stated by Samuels and Lambert,[11] who found marked discrepancies between the state of hyperplasia or aplasia of the marrow and the leucocyte content of the circulating blood in acute lobar pneumonia. Longcope[10] concluded upon the basis of experimental work on rabbits that the marrow cells become exhausted in fatal infections and it may be that a failure of the benzidine reaction may offer tangible evidence of such an exhaustion. But if the reaction should prove acceptable as such evidence, the condition of the marrow cells at death must be very different under different conditions since smears obtained from fatal infectious disease of various types may show a reaction on the part of the marrow cells fully as active as any found in non-infectious conditions. In fatal cases without myelocytic granule failure, therefore, and in the minor infectious conditions commonly encountered in which a variable deficiency may appear in the circulating leucocytes, it must be assumed that a cell emerging from the marrow with what may be considered as its normal granule content may subsequently undergo a more or less well-marked loss of the granular material. The conditions governing this loss have not been determined.

It may depend upon changes of a general nature in the blood as a whole as, for example, variations in the alkalinity, or it may indicate changes in the individual cell's functional activity or vital condition. The fundamental question underlying the whole problem is that as to the nature and significance of the granular substance and concerning this nothing is known.

In conclusion, the present study, while disregarding many fundamental questions that have suggested themselves, has concerned itself merely with the search for morphological variations in the leucocytes of the circulating blood as evident in their varying granule picture. The method available for the work suffers, in its present state of development, certain limitations and it may eventuate that these are serious enough to prevent the full acceptance of the indications derived from the limited amount of work here reported upon, but it is believed that, with due attention to the precautions noted, the method may serve to emphasize certain features not ordinarily considered in the study of the blood smear and that these features may prove to be of some interest if not of direct value in an immediate clinical sense. In another direction, the application of this or a corresponding method to the study of leucocytes engaged in phagocytosis either within the tissues or in the test tube might conceivably throw some light upon the mechanism involved in the leucocytic defense against toxic or bacterial agents.

Conclusions

The application of a benzidine staining method to blood smears suggests that the neutrophiles of the circulating blood have a characteristic granule content that appears to vary in health only within relatively narrow limits. In acute infectious diseases, and possibly in some other toxic conditions, these granules may lose their reactivity toward benzidine to more or less marked degree. The study of these granule changes may prove of interest through its bearing upon the general question of the leucocytic defensive mechanism and possibly through its more immediate employment as a practical aid in the clinical study of disease processes.

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Correspondence

"THE EVIL THAT HAS BEEN SPOKEN OF PHYSICIANS."

August 30, 1919.

DEAR MONT.—Letters from France have brought me the expression of Dr. Callemand's gratification because of the publication, in the ALBANY MEDICAL ANNALS, of the translations of extracts of some of his own articles and from his friend's work on the Evil that has been spoken of Physicians.

Another installment having been sent to you, it is fair to assume that he will be pleased to read it, as "more of the same" sort.

Hoping that the other readers of your "esteemed periodical" may feel as kindly toward these extracts as does our French colleague, I am always,

Yours cordially,

CULVER.

CICERO. "I hear it said, as you have written to me yourself, that your physician, Aesculapius, is held in high esteem; I do not, however, approve of his methods; I have taken care to let him know my opinion, on this point (XVI, 9).

. . . "I have written to Curius to give you the money of which you have need. I believe that you would better give something, also, to your physician, to make him more careful. (XVI, 4).

. . . "When two citizens had a suit, Verrius used to give them, as judges, according to his caprice, some of his attendants, a soothsayer, a towncrier or his physician, Cornelius. . . . What sort of men were these? They were a hungry gang that loafed in the king's vicinity, or, rather, they were dogs, such as you see licking the tribunal." (Act II, XIII.)

Oppianicus' mother-in-law finding herself somewhat indisposed, Oppi brought his physician to her service. . . . The woman cried that she didn't want attention from the man who had brought about the loss of all her family. But the unfortunate patient could not escape. . . . Her son-in-law addressed himself to a peripatetic empiric named L. Clodius. In return for a sum of four hundred sesterces, this quack took charge of the case; "He was in a hurry, he had several visits to make; he was brought to the patient, he gave her a potion and she soon expired."

. . . "A little while later, the physician, Strato, at S——, committed a theft and a murder. He strangled two slaves who were acting as guard of a treasure; but the crime was discovered and the guilty one perished on the cross, after having had his tongue cut out."

Piso, governor of Macedonia, not having been able to extort a certain sum of money from a deputy named Plato, had him thrown into prison and sent his physician to cut the captive's veins. This murder was accomplished with the most atrocious barbarity; Cicero cries: "What butchers they are, to employ their physicians, not to cure, but to kill!"

PETRARCH (1304-1374).

(As a prefatory note to fifty pages of abuse of physicians, by Plutarch, Dr. Witkowski says that, after having read all the "amenities" of the famous Italian author, anyone will agree with the French editor that the former needed a deal of "gaul" to write, in the first book of his *Invectives:* "It will not be found that I have said anything against medicine or reputable physicians; on the contrary, I have spoken only in favor of Hippocrates, against his enemies who decry his doctrine.")

The joke of Angelo, Bishop of Arezzo, on the doctors.

I'm going to tell you of an adventure of our Angelo, late Bishop of Arezzo, who belonged to the Ricasoli family. He was suffering from a serious indisposition; physicians who were called admonished him to take their drugs, saying that, otherwise he would run great risk of dying. Having a natural horror of drugging, he refused, at first; at length, however, moved by the begging of his friends, he promised to act on the doctors' prescriptions. As is usually the case, they sent him potions, for several days; these he poured in the chamber-pot and hid it under the bed. The doctors came to see him again, to note the effect of their drugs. They found that the fever had entirely left him, ascribed the cure to the use of their soi-disant remedies and reproached him with not having taken their potions earlier, when they would have immediately and entirely restored him—they said! The Bishop answered that the drugs must indeed have had admirable power and virtue since it had sufficed merely to

put them under his bed, with the resultant recovery of his health. "What would they have done if I had drunk them?" he asked: "Surely they would have made me immortal."

The second volume of *Le Mal qu'on a dit des Médecins* begins with an extract from the Fabliaux of the 13th century; it is called a Hippocratic Lay. Dr. Witkowski's note upon the story is that it would be hard to show a greater disregard for chronology and history than is evinced in this tale; that it was to Antonius Musa that a statue was erected, by the Athenians, because of his having saved Augustus' life; but that he was later held responsible for the death of Marcellus, the emperor's nephew, and that his statue was immediately torn down, in consequence. Hippocrates had so much the less chance to be concerned with this, because of his having been dead more than four hundred years when it happened.

. . . . . .

The author says that, before having acquired the celebrated reputation which has since immortalized him, having come to Rome during the reign of Augustus, he found the city in mourning for the emperor's nephew, who had just died; but that, having, at his own request, been brought to the palace, he poured into the corpse's mouth the juice of certain plants and thus brought the nephew back to life. The poet adds that Augustus, in recognition, caused two statues to be erected, of which one represented the nephew, the other the doctor; that he had them placed at the gate of the city, with an inscription which announced that Hippocrates, by his divine wisdom, had brought to life the quondam dead prince.

After Hippocrates had lived at Rome a few months, favored by the emperor, as he ought to have been, after rendering such a service and being almost adored by the people, as if he had been a god, a woman appeared on the scene and changed all this homage to laughter. She was a Gaul, of illustrious birth and rare beauty.

Augustus, who sought to treat her with distinction, had provided her with serving ladies and maids and, as a lodging, a house having a tower. As she wished to acquaint herself with the city's beauty and, with that purpose, went about it a great

deal, she came upon the statues in question and asked the occasion of their erection. This was explained to her; but the inscription had hardly been read to her when, bursting into hearty laughter, she answered: "I wasn't aware that Rome had a god in it and I am surprised that, under the circumstances, anyone dies, any more. Well, if they'll turn their little divinity over to me, for just one day, I'll bet my head that I'll make him the most ridiculous of men." As usual, this challenge was promptly reported to Hippocrates, whose *amour-propre* and curiosity were, naturally, piqued and aroused by it. He wanted to know this woman, who so confidently announced the power of her beauty; hence the chance to see her was sought by him. But it was his misfortune that he achieved that purpose, since she kept her promise only too thoroughly; for she was indeed beautiful and, in conversation, displayed so much grace and sprightliness that, despite all the spirit of opposition with which he was forearmed, she pleased him so much that he couldn't help falling in love with her. He fell so hard that it made him sick. The emperor came to see him; following this imperial example, ladies visited him, likewise and, finally, the stranger within the gates of that capital city, his lady-love, who readily and correctly diagnosticated his case. She sought and found a time when she was his sole visitor, when she asked him, in a most friendly tone, about his case. He, only too happy at having a chance to do so, made no bones about owning up that he was dying of love for her. That was what she wanted; Hence, affecting a tender interest in his illness and with seeming good faith, she said: "I should doubtless expose myself to much reproach and I should reproach myself much more if, being able to save a man of your merit I should be the cause of his demise. But even if I loved you as you love me, I leave it to yourself if it wouldn't be rather hard, under the circumstances, with so many eyes upon me as there are, to give you proofs of my affection. Be content, then, for the time being, with the expression of my regret and, with the assurance of my desire to prolong your life, receive the further assurance of my acceptance, in advance, of all means, of accomplishing that purpose, which your tenderness can furnish." So saying, she went out, as if blushing at the words she had just uttered. Hippocrates

derived from them hope and health, to the extent of being able soon to appear at the palace and resume his courtship of the beautiful Gaul.

"Well," she said to him, the first time that she saw him again: "Have you found any means of our becoming more nearly associated? What expedient have you discovered? Where are we at?" He answered that he had thought of the matter day and night, but that, up to that time, he had nothing to suggest. "You owe me gratitude, then" said she, "for, although I may not have exercised more ardor than you, in my quests, I have, at least, had more success. You know the tower in which I live; about the middle of the night be under its walls, with a basket that will hold you. For my part, with my cousin, whom I have succeeded in engaging on our side, I will let down to you, while my attendants are asleep, a rope to which you are to hitch your basket. When you have gotten into it, we will hoist you up and then, with no disturbance or fear, I hope to be able to give you proof of my affection."

Hippocrates was so blinded by his passion that this dull trap appeared to him the most adroit of stratagems. Thanking her profusely, he hurried away at once to buy the basket and was extravagantly impatient while awaiting the coming of the night. Finally, believing everybody asleep, he betook himself to the foot of the tower, with his basket and found—judge with what joy!—the rope already hanging out! He hitched the basket to it, and, getting into it, gave the signal to hoist away. And hoist away they did; but when he had reached a certain height, the dame made fast the cord to a hook; she left him hanging there and went away, wishing him quiet sleep and pleasant dreams.

Now, you know that, in those days, they had a peculiar custom in Rome, that for certain crimes, not punishable by death, the culprits were thus left hanging all day, from a tower, in a basket which, for that reason, was known as the convicts' basket.

When Hippocrates found himself thus trapped, he was in despair and cursed love and women a thousand times. There was nothing to do but pass the night in that place. Daylight only advertised his shame. In vain did he hide his face with his hands; everybody recognized him; a crowd gathered around and

all day long he was jeered and scoffed at by the populace. The guards about the tower, supposing that he was there by the emperor's orders, were careful not to rescue him from his predicament. That evening Augustus, returning from a hunt, and surprised to find someone in the basket without his orders, asked who it was. He was told that it was Hippocrates; he commanded that the doctor be lowered, at once, and announced, in anger, that he would avenge him thoroughly. But when he learned how it had come about that Hip had been fooled, he only laughed and, for a long time afterwards, all the barons had great fun with him about it.

Public Health

Edited by Arthur Sautter, M. D.

Department of Public Safety, Bureau of Health, Albany, N. Y.

Compiled by William F. Fullgraff, Registrar.

Bureau of Vital Statistics.

Deaths for Month of August, 1919.

Consumption	12	Bright's Disease	14
Typhoid Fever	1	Apoplexy	6
Scarlet Fever	0	Cancer	12
Whooping Cough	1	Accidents and Violence	14
Measles	0	Deaths under 1 year	13
Diarrheal Diseases	8	Deaths over 70 years	26
Pneumonia	1	Death rate	12.99
Broncho Pneumona	2	Death rate less non-residents	10.64

Deaths in Institutions

	Non-res.	Res.		Non res.	Res.
Albany Hospital	10	6	Public Places	1	1
Albany Hospital Camp	1	5	St. Margaret's House	1	2
Albany County Hospital	0	2	St. Peter's Hospital	3	11
Homeopathic Hospital	0	2			
Home for the Aged	2	2		23	38
Hospital for Incurables	1	2	Births		180
Maternity Hospital	2	3	Still Births		6

DIVISION OF COMMUNICABLE DISEASES

Typhoid Fever	2	Tuberculosis	31
Scarlet Fever	4	Mumps	1
Diphtheria and Croup	7	Pneumonia	4
Chickenpox	4	Influenza	1
Smallpox	0	Cerebro Spinal Meningitis	1
Measles	2		
German Measles	0	Total	67
Whooping-cough	10		

Number of days quarantine for scarlet fever:
Longest..... 32 Shortest..... 30 Average..... 31
Number of days quarantine for diphtheria:
Longest..... 10 Shortest..... 10 Average..... 10
Fumigations:
Rooms..... 105 Buildings..... 18
Milk bottles disinfected..... 222

MISCELLANEOUS.

Cards posted for communicable disease	5	Vaccinations	102
Cards removed	6	Vaccination dressings	76
Notices served on schools	0	Children examined for employment certificates	17
Notices served on stores and factories	2	Number of employment certificates issued	17
Postal card returns sent to doctors	13	Taking specimens of blood for Wassermanns	13
Postal card returns received from doctors	5	Taking specimens for Gonococci	12
Inspections and reinspections	7		

Tuberculosis.

Living cases on record August 1, 1919		872
Cases reported:		
By card	30	
Dead cases by certificate	4	34
		906
Dead cases previously reported	8	
Dead cases not previously reported	4	
Removed	1	
Died out of town	0	
Recovered	0	
Unaccounted for	0	13

Living cases on record September 1, 1919	893
Total tuberculosis death certificates	12
Non-resident deaths: Albany Hospital camp	1
Resident deaths	11
Visits to cases of tuberculosis	34
Miscellaneous visits	0
Visits to physicians	7

LABORATORY REPORT.

Diphtheria.

Initial Positive	19	Release Negative	10
Initial Negative	256	Unsatisfactory	5
Release Positive	35		
		Total	325

Sputum for Tuberculosis.

Positive	38	Unsatisfactory	0
Negative	84		
		Total	122

Widals.

Positive	2	Unsatisfactory	1
Negative	26		
		Total	29

Meningococcus

Positive	0	Negative	0
		Total	0

Wassermann tests	239	Gonorrhea examinations	57
Milk Analyses	237	Miscellaneous examinations	0
Water Analyses	0		
Pathological Examinations	0	Total examinations	1,009

DIVISION OF SANITATION.

Inspections	62	Reinspections	53
Plumbing	18	Plumbing	8
Sanitary	44	Sanitary	45

HEARINGS.

Hearings	5	Cases heard	5

Class of Cases

Filthy yard	2	Manure	1
Filthy premises	1	Privy vault	1

Disposition of Cases

Reinspection	5

DIVISION OF PLUMBING, DRAINAGE AND VENTILATION.

Inspections	121	Houses tested	14
Old houses	64	Smoke	0
New houses	57	Blue or red	0
Permits issued	54	Peppermint	3
Plumbing	41	Water test	11
Building	13	Houses examined	30
Plans submitted	22	Re-examined	64
Old buildings	11	Valid	12
New buildings	11	Without cause	18

REPORT OF REMOVAL OF DEAD ANIMALS.

Horses removed	25	Cats removed	117
Dogs removed	37		
		Total	179

DIVISION OF MARKETS AND MILK.

Public market inspections	4	Milk cans inspected	0
Market inspections	28	Milk cans condemned	0
Fish market inspections	2	Lactometer readings	70
Fish peddler inspections	0	Temperature readings	70
Slaughter house inspections	0	Fat tests	0
Rendering establishment inspections	0	Sediment tests	22
Pork packing house inspections	0	Chemical tests	0
Hide house inspections	0	Cows examined	513
Milk depots inspected	16	Cows quarantined	0
Stores inspected	38	Cows removed	7
Dairies inspected	47	Complaints investigated	5
		Milk houses inspected	47

Medical News

ALBANY GUILD FOR PUBLIC HEALTH NURSING — REPORT FOR MONTH OF SEPTEMBER, 1919.—Number of new cases, (167) 307; classified as follows: Charity cases, 58; cases moderate income, 37; metropolitan, 72; prenatal, no charge for calls, 31; dispensary social service, 56; tuberculosis, 79; venereal disease, 5. Cases carried from last month, 277; total cases carried during month, 584. New cases classified according to disease: Medical, 42; surgical, 46; obstetrical (a) prenatal, 31; (b) confinement, 32; (c) maternity, 7; miscarriages, 3; no diagnosis, 6; total, 167. Disposition:

Removed to hospital, 7; died, 12; cured, 51; improved, 47; unimproved, 19; discharged to other care, 4; discharged to dispensary, 11. Number of patients still under care, 433. Cases reported by: Physicians, 48; metropolitan agents, 36; patients, family or friends, 35; nurses, 34; S. S. department, (56) 3; other sources, 1; dispensary, 10; total, 167.

Visits for nurses (all departments.)—(Number of other visits, 377;) number of visits with treatment, 1,036; number of social service visits, 394; number of prenatal visits, 87; number of tuberculosis visits, 145; number of supervision visits, 107; total number of visits, 2,146.

Dispensary report.—Number of clinics held, 65; number of new patients, 64; number of old patients, 373; total number of patients treated during month, 446.

Classification of clinics held.—Prenatal, 10; surgical, 13; nose and throat, 1; eye and ear, 18; skin and G. U., 4; medical, 8; tuberculosis, 4; venereal, 4; lung, see t. b.; dental, 0; neurological, 2; stomach, 0; pediatrics, 5; gynecological, 6.

Special tuberculosis department.—Number of tuberculosis patients sent to hospital, 2; number of tuberculosis patients returned from hospital, 2; number of tuberculosis patients died, 6; number of tuberculosis patients assisted with milk and eggs, 6.

Special venereal disease department.—New patients, 4; old, patients, 59; number of Wassermanns, 11; number of smears, 1; sounds passed, 0; Salversan treatments, 33; Binoide treatments, 11; Hg. Salicylate treatments, 10. Total treatments, 54.

Operations and treatments.—Parafine dressing to burned arm; hand sutured; abscess on buttocks incised and drained; abscess on head incised and drained; chalazon incised; abscess on wrist incised; ears irrigated; finger incised and drained.

F. R. Freeman,
Superintendent.

French Campaign Against Tuberculosis.— French methods to combat the spread of tuberculosis which had gained a strong foothold in the country were practically nullified by the war until the American Red Cross came to the aid of the people.

Through the agencies of the organization there is now a capacity for 1,983 bed patients in the tuberculosis hospitals in Paris and outside of Paris there are accommodations for 5,610.

The Bureau of Tuberculosis is working in close conjunction with the Rockefeller Commission for the Prevention of Tuberculosis in France. The total number of beds assisted by the Red Cross Bureau of Tuberculosis amounted to 24,185. They were aided to the extent of 3,287,417 francs and relief was supplied to the extent of 794,447 francs.

An appropriation for a Serbian hospital in Paris has been made because it was found, after examination, that twenty per cent of the 200,000 Serbs studying in the country were tubercular.

TENTS AS HOSPITALS.—Tents as hospitals was a wartime emergency in France which resulted very favorably. Because of the scarcity of wood, tents were established as hospitals by the Forty-second and Seventy-seventh Divisions, each using nine tents. At the Steeple Chase grounds at Autueil, the American Red Cross placed thirty-nine tents as wards. They had wooden frames and floors and were ventilated by means of eighteen windows. It required six or seven hours with a crew or five or six men to erect such a hospital. When the armistice was signed, the Red Cross was preparing to establish a tent hospital consisting of one hundred and eleven tents.

TYPHUS RAGING IN EUROPE.—An epidemic of typhus is raging in Europe and the Red Cross is taking an active part in the effort to stamp out the disease.

Henry P. Davidson reports that 275,000 cases have been found in the belt extending from the Baltic to the Black sea and there is appalling distress in Poland, Lithuania and the Balkans.

The Red Cross has sent 200 representatives to Poland in response to a pathetic appeal from Paderewski. Edicts calculated to stop the spread of the disease have been published in that country, one of them being an order that every person shave and bathe. About 100,000 cases have been reported and the death rate is high.

At the conference held in Cannes, recommendations were made to enlist Red Cross Societies to establish a permanent committee of medical experts of the allied countries to deal with the typhus problem.

NURSING SCHOOLS OPENED IN BUFFALO.—A post-graduate course for public health nurses is to be given in Buffalo for sixteen weeks beginning September 29th, under the auspices of the Buffalo University, the Buffalo Chapter of the American Red Cross, the Department of Health, the District Nursing Association, and the Department of Hospitals and Dispensaries.

An excellent teaching staff has been secured. A certificate will be given to all students satisfactorily completing the course, which will cost $25.00. The class will be limited to thirty, and applicants must be registered in New York State or states having equivalent standards. Application blanks will be supplied by the University of Buffalo, College of Arts and Sciences, Niagara Square, Buffalo, New York.

MARRIED.—Dr. BYRON G. SHULTS (A. M. C. '15) and Miss FRANCES BENNETT were married at Chillicothe, O., August 31, 1919. Dr. Shults had served in the Army Medical Corps, with rank as captain, and had received his honorable discharge two weeks before the marriage. Dr. and Mrs. Shults will live in Johnstown, N. Y.

PERSONAL.—Dr. ELMER HARRISON ORMSBY (A. M. C. '13) has been honorably discharged from Medical service, and has resumed his practice of medicine and surgery at 33 Church Street, Amsterdam, N. Y.

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Recent Accessions.

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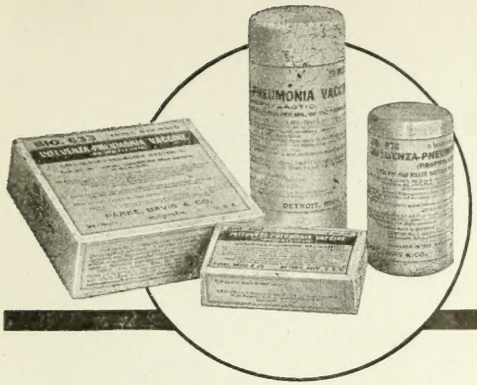

Prophylaxis of Influenza

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Bio. 633. 3 syringes.
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IF, as now seems probable, there is to be a recurrence this fall and next winter of the scourge which a few months ago exacted a toll of half a million lives in this country, what means can be taken to limit a spread of the disease and to lessen its fatalities?

Immunization with a reliable preventive vaccine undoubtedly offers the most practical and promising measure within the reach of physicians.

While from data thus far available it cannot be definitely asserted that the protective value of influenza vaccine is as fully determined as is that of smallpox or typhoid vaccine, there is abundant evidence that it reduces susceptibility to infection and modifies the severity of the disease when the patient is attacked; furthermore, few of those attacked develop pneumonia.

Influenza-Pneumonia Vaccine (Prophylactic) is offered to the medical profession with confidence in its efficacy as an immunizing agent. It is prepared after the formula of Dr. Rosenow and contains five billion organisms in one mil (16 minims).

The vaccine is administered in three graduated doses at intervals of three or four days. The first dose (adult) is ½ mil (8 minims); the second, 1 mil (16 minims); the third, 1½ mils (24 minims). The doses for children are one-third to one-half of those here specified.

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Quinine and strychnine in small but continued doses exert a "dynamic" or activating influence upon all metabolism.

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